

CLAIMS

1. A method for identifying a substance that down-regulates an immune response in an animal, comprising determining whether said substance inhibits an interaction between factors in the CD26 signaling pathway.

5 2. The method of claim 1, comprising determining whether said substance inhibits:

- (a) the interaction between CD26 and caveolin-1;
- 10 (b) the interaction between caveolin-1 and Tollip; or
- (c) the interactions between caveolin-1, Tollip, and IRAK-1.

15 3. The method of claim 1 or 2, wherein said interaction(s) are protein:protein binding.

20 4. The method of any one of claims 1-3, wherein said interaction(s) are determined by one or more assay(s) selected from the group consisting of immunoprecipitation, Western blotting, affinity chromatography, fluorescence microscopy, and two hybrid assay.

25 5. The method of claim 1, comprising determining whether said substance inhibits:

- (a) the phosphorylation of caveolin-1;
- (b) the phosphorylation of IRAK-1;
- 25 (c) the activation of NF-κB; or
- (d) the up-regulation of CD86 expression.

30 6. The method of any of claims 1-5, comprising contacting cells or extracts from cells with said substance.

7. The method of claim 6, wherein said cells are T cells or monocytes.

35 8. The method of claims 6 or 7, wherein said cells recombinantly express a factor in the CD26 signaling pathway.

9. The method of any one of claims 6-8, wherein said cells comprise a

reporter gene the expression of which is responsive to a factor in the CD26 signaling pathway.

10. The method of any of claims 1-9, wherein said substance is part of a library  
5 of substances.

11. A kit for identifying a substance that down-regulates an immune response  
in an animal, comprising at least one agent which may be used to determine the level or  
function of at least one factor in the CD26 signaling pathway.

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12. The kit of claim 15, comprising at least one agent for determining whether  
a substance inhibits:

- (a) the interaction between CD26 and caveolin-1;
- (b) the interaction between caveolin-1 and Tollip;
- 15 (c) the interactions between caveolin-1, Tollip, and IRAK-1;
- (d) the phosphorylation of caveolin-1;
- (e) the phosphorylation of IRAK-1;
- (f) the activation of NF-κB; or
- (g) the up-regulation of CD86 expression.

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13. Use of an immunoregulatory agent that inhibits the CD26 signaling  
pathway in the manufacture of a medicament for treating, ameliorating, or preventing a  
disorder related to an immune response in an animal.

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14. The use of claim 13, wherein said immunoregulatory agent inhibits:  
(a) the interaction between CD26 and caveolin-1;  
(b) the interaction between caveolin-1 and Tollip;  
(c) the interactions between caveolin-1, Tollip and IRAK-1;  
(d) the phosphorylation of caveolin-1; or  
30 (e) the phosphorylation of IRAK-1.

15. The use of claim 13, wherein said immunoregulatory agent is a small  
interfering RNA (siRNA).

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16. The use of claim 15, wherein said siRNA is targeted to caveolin-1 or  
Tollip.

17. The use of claim 16, where said siRNA comprises the sequence of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:9, or SEQ ID NO:10.

5 18. The use of any of claims 13-17, further comprising administering an additional therapeutic agent.

19. The use of any of claims 13-18, wherein said disorder in need of immune suppression is an autoimmune disorder, an inflammatory disorder, or transplant rejection.

10 20. A pharmaceutical composition comprising an immunoregulatory agent that inhibits the CD26 signaling pathway and a pharmaceutically acceptable carrier.

15 21. The pharmaceutical composition of claim 20, wherein said immunoregulatory agent is an siRNA.

22. The pharmaceutical composition of claim 21, wherein said siRNA is targeted to caveolin-1 or Tollip.

20 23. The pharmaceutical composition of claim 22, where said siRNA comprises the sequence of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:9, or SEQ ID NO:10.

24. A siRNA targeted to caveolin-1 or Tollip.

25 25. The siRNA of claim 24, where said siRNA comprises the sequence of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:9, or SEQ ID NO:10.

30 26. A method for treating, ameliorating, or preventing a disorder related to an immune response in an animal, comprising administering to an animal in need thereof a substance that inhibits an interaction between factors in the CD26 signaling pathway.

27. A method for identifying a substance that up-regulates an immune response in an animal, comprising determining whether said substance enhances an interaction between factors in the CD26 signaling pathway.

35 28. The method of claim 27, comprising determining whether said substance enhances:

- (a) the interaction between CD26 and caveolin-1;
- (b) the interaction between caveolin-1 and Tollip; or
- (c) the interactions between caveolin-1, Tollip, and IRAK-1.

5           29. The method of claim 27, comprising determining whether said substance  
enhances:  

- (a) the phosphorylation of caveolin-1;
- (b) the phosphorylation of IRAK-1;
- (c) the activation of NF- $\kappa$ B; or
- 10          (d) the up-regulation of CD86 expression.

30. A kit for identifying a substance that up-regulates an immune response in  
an animal, comprising at least one agent which can be used to determine the level or function  
of at least one factor in the CD26 signaling pathway.

15           31. The kit of claim 30, comprising at least one agent for determining whether  
a substance enhances:  

- (a) the interaction between CD26 and caveolin-1;
- (b) the interaction between caveolin-1 and Tollip;
- 20          (c) the interactions between caveolinin-1, Tollip, and IRAK-1
- (d) the phosphorylation of caveolin-1;
- (e) the phosphorylation of IRAK-1;
- (f) the activation of NF- $\kappa$ B; or
- (g) the up-regulation of CD86 expression

25           32. Use of an agent that enhances the CD26 signaling pathway in the  
manufacture of a medicament for treating, ameliorating, or preventing a disorder related to  
an immune response in an animal.

30           33. The use of claim 32, wherein said agent enhances:  

- (a) the interaction between CD26 and caveolin-1;
- (b) the interaction between caveolin-1 and Tollip;
- (c) the interactions between caveolin-1, Tollip and IRAK-1;
- (d) the phosphorylation of caveolin-1; or
- 35          (e) the phosphorylation of IRAK-1.

34. A pharmaceutical composition comprising an agent that enhances the CD26 signaling pathway and a pharmaceutically acceptable carrier

35. A method for treating, ameliorating, or preventing a disorder related to an immune response in an animal, comprising administering to an animal in need thereof a substance that enhances an interaction between factors in the CD26 signaling pathway.